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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/821,657	WADA ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *5,7,45-50,80 and 82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-44,51-79,81 and 83-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Claims 1-44 and 51-93 and the species heparin sulfate in the reply filed on 4/28/2006 is acknowledged.

2. Claims 1-93 are pending, Claims 45-50 are withdrawn from consideration as being drawn to a nonelected invention. Claims 5, 7, 80, and 82 are withdrawn as being drawn to a nonelected species (polycatonic).

3. An action on the merits for Claims 1-44 and 51-93 is set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 30-32, 39-41, 52, and 54-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30-32 recites the limitation "further comprises" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 28 is drawn to a separation media but the claim does not describe what the media comprises therefore it is unclear what would "further comprise".

Claims 39-41 are unclear with regard to which analyte is labeled. Claim 39 is drawn to contacting a sample containing the analyte with the analyte labeled by a

detectable marker or an analogue of the analyte. It is unclear if there are two separate analytes, a sample analyte and a labeled analyte, or if the sample analyte is labeled.

Claim 42 is unclear with regard to what the sample containing the analyte is contacting. It is unclear if the sample containing the analyte is contacting: an analyte bound to a charged carrier molecule OR an analogue of the analyte bound to a charged carrier molecule and one or more affinity molecule labeled by a detectable marker to form a first complex OR the analogue bound to a charged carrier molecule and the labeled affinity molecule and a second complex of the analyte in the sample and the labeled affinity molecule. Or if the sample containing the analyte is contacting: an analyte bound to a charged carrier molecule OR an analogue of the analyte bound to a charged carrier molecule, then either the analyte bound to the charged carrier or the analyte AND one or more affinity molecule labeled by a detectable marker to form a first complex OR the analogue bound to a charged carrier molecule and the labeled affinity molecule and a second complex of the analyte in the sample and the labeled affinity molecule. It is unclear which combinations are needed for contacting the sample. Further, it is unclear if the analyte is the same from the sample or if it's another analyte.

Claim 52 is unclear. With regard to Claim 52, it is unclear what is "lower"; it is unclear if the noise constituent is lower than the complex or lower than in the original solution. It is further unclear what "is concentrated". Is the complex concentrated or is the noise constituent concentration. Claim 52 recites the limitation "the concentration of a noise constituent" in line 2. There is insufficient antecedent basis for this limitation in the claim

Claim 54 is unclear. Claim 54 is drawn to concentrating the complex wherein the buffer in the concentration channel slows electrophoretic mobility of the complex as compared to the complex in a solution that contains the complex. Is the complex slower in the buffer than in the solution? It is unclear if the solution is added to the buffer how only the complex could be affected by the buffer. It is unclear how the buffer slows electrophoresis. Further, the term "slower" in claim 54 is a relative term, which renders the claim indefinite. The term "slower" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 55 recites the limitation "the noise constituents" in line 2. There is insufficient antecedent basis for this limitation in the claim

Claim 56 recites the limitation "the noise constituents" in line 2. There is insufficient antecedent basis for this limitation in the claim

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3, 6, 9-29, 33, 35-44, 51-55, 59-65, 67, 68-78, 81, 83, 85-86, 90, and 92-93 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawabata et al. (EP 1376126A1 3/04/2002) as evidenced by Walston et al. (US Patent Application Publication 2001/0055591 December 27, 2001).

CLAIM 1 is an independent Claim.

With regard to Claim 1, Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity substances in the separation method (p. 23 paragraphs 144-145). Walston et al. defines heparin is a polysaccharide with a strong negative charge (p. 2 paragraph 0016). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches using heparin to block nucleases to inhibit digestion therefore reducing the interference from Dnase and Rnase (p. 23 paragraphs 144-145). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Claims 2-3, 6, 9-13, 22, 27, 35-36, 43-44 depend from Claim 1

With regard to Claims 2-3, and 6, Kawabata et al. teaches using heparin (p. 23 paragraphs 144-145). Walston et al. teaches heparin is a polysaccharide with a strong negative charge (p. 2 paragraph 0016).

With regard to Claims 9 and 22, Kawabata et al. teaches a nucleic acid chain affinity substance is labeled with a marker (Figure 2). With regard to Claims 11, 12, and 13, Kawabata et al. teaches the binding of "protein" and "peptide chain"; "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 6 paragraph 20).

With regard to Claim 10, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (analyte) (Figure2). Claims 16-18 defines nucleic acids as having a negative charge. Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

With regard to Claim 27, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 8 paragraph 26).

With regard to Claim 35, Kawabata et al. teaches the diameter of the capillary channel (cross sectional microscale dimension) of between 1 to 200 microns (p. 12 paragraph 58).

Claims 14-21, 23-26, 28-29, 33, 37, and 38 depend from Claim 10

With regard to Claim 14, Kawabata et al. teaches the charged carrier molecule is a nucleic acid chain (anionic) (p. 3-4 paragraph 6). With regard to Claim 15, the

charged carrier molecule is a nucleic acid chain (negative charge) and the charged polymer is a heparin (negative charge).

With regard to Claims 16-17, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6).

With regard to Claims 18, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15). With regard to Claims 19-21, Kawabata et al. teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) (p. 7 paragraph 22 and p. 9 paragraph 32).

With regard to Claims 23-24, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance. With regard to Claim 25, Kawabata et al. teaches the nucleic acid chain is labeled (Figure 2).

Claim 26 is drawn to an affinity molecule in the conjugate, which is labeled by a detectable marker. The claim is not limited to a label, which is directly connected to the affinity or directly connected with a linker to an affinity. Therefore, since in the conjugate the nucleic acid is directly attached to the affinity and the nucleic acid is labeled the affinity would be labeled. Kawabata et al. teaches a method using an Alexa488-labeled anti-AFP antibody Fab' fragment (p. 24 p. 152).

With regard to Claim 28, Kawabata et al. teaches separating the complex using capillary electrophoresis (p. 12 paragraph 58). With regard to Claim 29, Kawabata et al.

teaches the separation media can be comprised of polyethylene glycol, polyacrylamide, polyethylene oxide, or polyvinylpyrrolidone (p. 12, paragraph 59).

With regard to Claim 33, Kawabata et al. teaches using heparin in a solution containing the target (p. 23 paragraphs 144-145). Walston et al. teaches heparin is a polysaccharide with a strong negative charge (p. 3 paragraph 5).

With regard to Claim 36, Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 74). Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).

With regard to Claim 43, Kawabata et al. teaches targets comprising serum, plasma, urine, feces, and environmental samples (p. 11 paragraph 49). With regard to Claim 44, Kawabata et al. teaches a target comprising AFP, FSH, TSH, LH, HIV, CA10-19, CA125, PSA, or T4 (p. 5 paragraph 56).

Claim 37 has every limitation of Claim 10, but also includes the limitation that two or more conjugates are used wherein each affinity molecule is capable of binding the analyte at a different site. Kawabata et al. teaches at least two affinity molecules (in a complex) which bind to the target (analyte) at different sites (Figure 4).

Claim 38 has every limitation of Claim 10, but also the limitation that the affinity molecule and the affinity molecule in the conjugate have a property capable of binding

to the analyte at a different site on the analyte form every other affinity molecule. Kawabata et al. teaches a method in which the nucleic acid (charged carrier molecule), affinity molecules, and analytes are in a solution together (Figure 2). Kawabata et al. teaches at least two affinity molecules (in a complex) which bind to the target (analyte) at different sites (Figure 4).

Claim 39 is an independent Claim and Claims 40-41 depend from Claim 39

With regard to Claims 39-41, Kawabata teaches a method in which an anlayte, affinity, and a charge polymer form a complex which is labeled (first complex) (Figure 6). The claim does not limit how the analyte is labeled so therefore a conjugate comprising the analyte, affinity, and a labeled charged polymer would encompass the claims. Kawabata et al. teaches 2 or more of these complexes can be made (Figure 6). Kawabata et al. teaches separating the sample (Figure 6). Kawabata et al. teaches 2 or more affinity molecules can be used (Figure 6). Kawabata et al. teaches measuring and determining the amount of analyte in the sample (Abstract).

Claim 42 is an independent Claim

With regard to Claim 42, it is unclear in the claim which combination is actually needed in the first complex. With regard to the first complex, Kawabata et al. teaches contacting the sample with a complex of analyte, affinity, and detectable marker (figure 2). Since the analyte is labeled in this complex because of the attachment of the labeled charged molecule it is unclear what the difference it between the first and second complex. Kawabata et al, teaches 2 or more types of targets can be labeled

(forming 2 or more complexes) and separated (Figure 6). Further Kawabata et al. teaches that two ore more affinity molecules may be used in the separation (Figure 6).

Claim 51 is an independent Claim.

With regard to Claim 51, Kawabata et al. teaches contacting a sample, with an affinity attached to a nucleic acid chain, which is labeled (Figure 2). Kawabata et al. teaches separating the complex using capillary electrophoresis (p. 12 paragraph 58). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Claims 52-55, 59-65, 67, 68-78, 81, 83, 85-86, 90, and 92 depend from Claim 51

With regard to Claim 52, the specification does not define noise constituent. Kawabata et al. teaches a separation of the conjugate from the nucleic acid chain-binding affinity substance-marker not involved in the formation of the complex. Therefore in separating the conjugate not in the complex from the complex the

concentration of the noise constituent is lowered. The noise constituent is anything that is not in the complex.

With regard to Claim 53, Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Therefore the complex goes through a concentration channel (first capillary) and then to the separation capillary in a solution stopping at a reservoir between the two capillaries (microchannel fluidically).

With regard to Claim 54, it is unclear how the buffer affects the sample. Kawabata et al. teaches buffers for use in migration including tris, phosphate, Veronal, borate, Good's, SSC, TBE and TAE (p. 12 paragraph 63).

With regard to Claim 55, Kawabata et al. teaches that retention time (electrophoretic mobility) was different between the labeled conjugate and the antibody alone (noise constituents) (p. 27 paragraph 170). Kawabata et al. teaches that separation ability is improved with the use of a charged substance (p. 2-3 paragraph 9).

With regard to Claims 59-61, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6). With regard to Claim 62, Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15). With regard to Claims 63-65, Kawabata et al.

teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) (p. 7 paragraph 22 and p. 9 paragraph 32).

With regard to Claim 67, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). With regard to Claims 68-69, Kawabata et al. teaches the binding of "protein" and "peptide chain"(protein: protein interaction); "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 6 paragraph 20). With regard to Claim 70, Kawabata et al. teaches the affinity molecule can be FAB, $F(ab')_2$ (p. 6 paragraph 21).

With regard to Claim 71, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance.

Claim 74 is drawn to an affinity molecule in the conjugate, which is labeled by a detectable marker. The claim is not limited to a label, which is directly connected to the affinity or directly connected with a linker to an affinity. Therefore, since in the conjugate the nucleic acid is directly attached to the affinity and the nucleic acid is labeled the affinity would be labeled. Kawabata et al. teaches a method using an Alexa488-labeled anti-AFP antibody Fab' fragment (p. 24 paragraph 152).

With regard to Claims 72-73, Kawabata et al. teaches an affinity attached to a nucleic acid chain, which is labeled (Figure 2). With regard to Claim 75, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 8 paragraph 26).

With regard to Claim 76, Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity substances (p. 23 paragraphs 144-145). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Therefore Kawabata et al. teaches a solution with a charged polymer added to a concentration channel.

With regard to Claim 77-78, Kawabata et al. teaches using heparin in a solution containing the target (p. 23 paragraphs 144-145). Walston et al. teaches heparin is a polysaccharide with a strong negative charge (p. 3 paragraph 6).

With regard to Claim 81, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2).

With regard to Claim 83, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) and heparin (charged polymer) (Figure 2, p. 23 paragraphs 144-145). Both the nucleic acid chain and heparin are negatively charged.

With regard to Claims 85-86, Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying

voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Kawabata et al. teaches the capillary is filled with a filler such as, polyethylene glycol, polyethylene oxide, polyvinylpyrroliodone, and polyacrylamide (p. 12 paragraph 59). With regard to Claim 90, Kawabata et al. teaches a nuclease inhibitor such as heparin is added to the sample solution (p. 23 paragraph 144-145). Walston et al. teaches heparin is a polysaccharide with a strong negative charge (p. 3 paragraph 6).

With regard to Claim 92, Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

Claim 93 is an independent Claim

With regard to Claim 93, Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13, paragraph 74). Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity

substances in the separation method (p. 23 paragraphs 144-145). Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity substances in the separation method (p. 23 paragraphs 144-145). Walston et al. teaches heparin is a polysaccharide with a strong negative charge (p. 3 paragraph 5). Kawabata et al. teaches using heparin to block nucleases to inhibit digestion therefore reducing the interference from Dnase and Rnase (p. 23 paragraphs 144-145). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 4, 8, 79, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Bickel et al. (Proceedings of Natl. Acad. Sci. November 1992 Vol. 89 p. 10001).

Kawabata et al. teaches all the limitations of the independent Claims of 1 and 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target

substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (Column 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity substances (p. 23 paragraphs 144-145). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is

introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Therefore Kawabata et al. teaches a solution with a charged polymer added to a concentration channel.

Kawabata et al., however, is silent with regard to if the heparin is heparin sulfate.

Bickel et al. teaches a method of detecting specific RNA-protein complexes on a polyacrylamide gel with inhibitors (Figure 1 paragraph p. 10002). With regard to Claims 4, 8, 79, and 84 Bickel et al. teaches using heparin sulfate as a nonspecific competitor in an SDS gel (p. 10003 1st column 1st paragraph and Figure 3).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include heparin sulfate as a nonspecific competitor as taught by Bickel et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include heparin sulfate as a nonspecific competitor as taught by Bickel et al., because Bickel et al. teaches the addition of heparin sulfate made the complex migrate more rapidly and simplified the pattern of proteins on the SDS gels (p. 1005 1st paragraph). Bickel et al. teaches heparin increases the intensity of faint bands (p. 1005 1st paragraph).

7. Claims 30-32 and 87-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Stathakis et al. (Journal of Chromatography A 1998 Vol. 817 p. 227).

Kawabata et al. teaches all the limitations of the independent Claims of 1 and 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (Column 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore,

the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

Kawabata et al., however, does not teach a separation media which comprises a charged polymer.

With regard to Claims 30 and 87, Stathakis et al. teaches a coating on the capillary electrophoresis silca fuse glass, which contains dextran sulfate or polyvinyl suphonic acid (PVS) (abstract and p. 230 2nd column Section 3.3). With regard to Claims 31-32 and 88-89, Stathakis et al. teaches a method using 0.001-0.1% dextran or 0.001-1% PVS (p. 230 last paragraph).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include charged polymers in separation media as taught by Stathakis et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include charged polymers in separation media as taught by Stathakis et al., because Stathakis et al. teaches polymers incorporated in the separation buffer can improve migration time reproducibility (p. 229 2nd column 1st sentence).

8. Claims 34 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Stalcup et al. (Analytical Chemistry 1994 Vol. 66 p. 3054).

Kawabata et al. teaches all the limitations of the independent Claims of 1 and 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

Kawabata et al. teaches adding heparin (charged polymer) to the solution of nucleic acid chain-binding affinity substances in the separation method (p. 23

paragraphs 144-145). Kawabata et al. teaches using heparin to block nucleases to inhibit digestion therefore reducing the interference from Dnase and Rnase (p. 23 paragraphs 144-145). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Kawabata et al., however, is silent with regard to the concentration to heparin in the buffer.

With regard to Claim 34 and 91, Stalcup et al. teaches using 2% heparin in the phosphate buffer in capillary zone electrophoresis (abstract).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include 2% concentration or charged polymers in a buffer as taught by Stalcup et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include 2% concentration or charged polymers in a buffer as taught by Stalcup et al., because Stalcup et al. teaches the highly anionic character of heparin enhances its aqueous solubility while offering the potential for considerable electrophoretic mobility and therefore has utility as a chiral mobile phase additive in capillary zone electrophoresis (p. 3054 1st column 2nd paragraph).

9. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Fukui et al. (Nucleic acid Research, 1996 Vol. 24 p. 3962).

Kawabata et al. teaches all the limitations of the independent Claim 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore,

the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15). Kawabata et al. teaches the use of ACMA as a marker (p. 8 paragraph 27).

Kawabata et al., however, does not teach a synthetic sequence consisting of a nucleotide that contains a methylene group in the place of the oxygen in the ribose ring.

Fukui et al. teaches linking ACMA to DNA (abstract). With regard to Claim 66, Fukui et al. teaches the ACMA is connecter through a tri-pentamethylene linker (Abstract). Therefore, Fukui et al. teaches a synthetic sequence consisting of a linker, which has a methylene group.

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include methylene linker as taught by Fukui et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include methylene linker as taught by Fukui et al., because Fukui et al. teaches a pentamethylene linker which stabilizes the connection between ACMA and the DNA (Abstract).

10. Claims 57-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Kaniansky et al. (Analytical chemistry 2000 Vol. 72 p. 3596).

Kawabata et al. teaches all the limitations of the independent Claim 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (Column 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58).

Kawabata et al. teaches contacting a sample, with an affinity attached to a nucleic acid chain, which is labeled (Figure 2). Kawabata et al. teaches separating the complex using capillary electrophoresis (p. 12 paragraph 58). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less

(p. 11-12 paragraph 54). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7).

Kawabata et al., however, does not teach the concentration using isotachophoresis (ITP).

With regard to Claims 57-58, Kaniansky et al. teaches a method of using a capillary electrophoresis chip with a two separation channel coupling (Abstract). Kaniansky et al. teaches using ITP as a concentration pretreatment of the analyte (Abstract).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include the ITP concentration method as taught by Kaniansky et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include the ITP concentration method as taught by Kaniansky et al. because Kaniansky et al. teaches using an ITP concentration pretreatment quantified test analytes by 1-2% RSD (Abstract). Kaniansky et al. teaches

a well-defined ITP concentration of the analyte can be integrated into the separation method of a capillary channel chip (Abstract).

11. Claims 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) in view of Wolfe et al. (Electrophoresis March 23, 2002 Vol. 23 p. 727).

Kawabata et al. teaches all the limitations of the independent Claim 51 as presented in the 102 rejection stated above. Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (Column 13, paragraph 74). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58).

Kawabata et al. teaches contacting a sample, with an affinity attached to a nucleic acid chain, which is labeled (Figure 2). Kawabata et al. teaches separating the complex using capillary electrophoresis (p. 12 paragraph 58). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the

sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation, therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (anlayte) (Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7).

Kawabata et al., however, does not teach the concentration based on adsorption of the charged carrier.

With regard to Claims 56-57, Wolfe et al. teaches the incorporation of a silica-based solid phase extraction (SPE) system into a microchip platform (the same platform described by Kawabata et al) (Abstract). Wolfe et al. teaches the extraction procedure utilizes the adsorption of DNA onto bare silica (abstract). Wolfe et al. teaches that DNA is removed from the sample load solution and is retained in the washing step (p. 732 1st column last paragraph). Therefore DNA is adsorbed while "noise constituents" are washed away.

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of

Kawabata et al. to include the SPE concentration method as taught by Wolfe et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include the SPE concentration method as taught by Wolfe et al. because Wolfe et al. teaches a method of concentrating DNA (so therefore the charged carrier attached to the affinity molecule and the analyte) from noise constituents in the sample by adhering the DNA onto a silica wall (Abstract). The ordinary artisan would be motivated to use the SPE concentration method because Wolfe et al. teaches the extraction of nanogram quantities of DNA in less than 25 minutes (abstract). The ordinary artisan would be motivated to concentrate the charge carrier, affinity, and analyte from noise constituents in a fast and efficient manner.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon 7/19/06

Katherine Salmon
Examiner
Art Unit 1634

BJ FORMAN, PH.D.
PRIMARY EXAMINER